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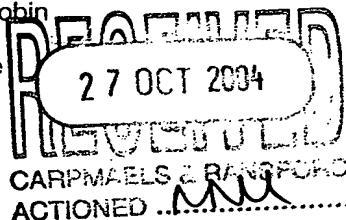
DUE: 25.1.05

PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

WRITTEN OPINION  
(PCT Rule 66)

Applicant's or agent's file reference <b>P032789WO</b>		Date of mailing (day/month/year)	25.10.2004
International application No. <b>PCT/GB 03/05651</b>		International filing date (day/month/year)	24.12.2003
		Priority date (day/month/year)	24.12.2002
International Patent Classification (IPC) or both national classification and IPC <b>C07D417/04</b>			
Applicant <b>METRIS THERAPEUTICS LIMITED et al.</b>			

- This written opinion is the **first** drawn up by this International Preliminary Examining Authority.
- This opinion contains indications relating to the following items:
  - ☒ Basis of the opinion
  - ☐ Priority
  - ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - ☐ Lack of unity of invention
  - ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - ☐ Certain documents cited
  - ☐ Certain defects in the international application
  - ☐ Certain observations on the international application
- The applicant is hereby **invited to reply** to this opinion.
 

**When?** See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

**How?** By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

**Also:** For an additional opportunity to submit amendments, see Rule 66.4.  
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.  
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.
- The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 24.04.2005

Name and mailing address of the international preliminary examining authority:



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**I. Basis of the opinion**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*):

**Description, Pages**

1-56 as originally filed

**Claims, Numbers**

1-46 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

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☐ the entire international application,

☒ claims Nos. 37,41-46

because:

☒ the said international application, or the said claims Nos. 37,41,42 relate to the following subject matter which does not require an international preliminary examination (specify):

**see separate sheet**

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 43-46 are so unclear that no meaningful opinion could be formed (*specify*):

**see separate sheet**

☒ the claims, or said claims Nos. 43-46 are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the Standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

### V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

#### 1. Statement

Novelty (N)	Claims	
Inventive step (IS)	Claims	1-36,38-40
Industrial applicability (IA)	Claims	

#### 2. Citations and explanations

**see separate sheet**

**SECTION III**

- 1). Claims 37,41,42 relate to the treatment of human and/or animal bodies. According to Rule 67(1)(iv) an examination is not required for such claims.
- 2). Claims 43-46 relate to indefinite compounds whose structure is not available or described in the description.
- 3). Claims 43-46 concern any compound having the VEGF inhibitory properties. Since the description does not contain enough information allowing the skilled person to reproduce all these compounds, these claims render the current application not reproducible.

**SECTION V**

- 4). Relevant prior art is represented by:

D1: WO 99/00356 A (GONG YONG ;KLEIN SCOTT I (US); PAULS HEINZ W (US); GUERTIN KEVIN R) 7 January 1999 (1999-01-07)  
D2: WO 95/33050 A (SHARKEY ANDREW MARK ;SMITH STEPHEN KEVIN (GB); LYNXVALE LTD (GB);) 7 December 1995 (1995-12-07)  
D3: US-A-3 966 748 (SAFIR SIDNEY ROBERT ET AL) 29 June 1976 (1976-06-29)

- 5). None of the cited documents describes a compound having the specific substituted five-membered rings of the left-hand side of the molecule. Novelty is thus acknowledged.

- 6). None of the cited documents describes compounds having the same pharmaceutical properties as those currently claimed.

Therefore, the problem underlying the current application is the provision of alternative compounds useful to treat endometriosis.

The data of the description show that this problem has been solved by the tested compounds.

However, due to the presence of unlimited expressions in the wording of the claims

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SEPARATE SHEET**

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(see: optionally substituted, aryl, alkyl, pharmaceutically acceptable derivatives and derivatives thereof), it cannot be assumed that an unlimited and sometime snot defined compounds will solve the given problem.

Thus, an inventive step on the whole claimed scope is not acknowledged.

7). For the assessment of the present claims 37,41,42 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.